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PRE-APPEAL BRIEF REQUEST FOR REVIEW

Docket Number (Optional)
1599-0293PUS1

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Application Number	Filed
10/554,637	October 27, 2005

First Named Inventor
Min-Hyo SEO

Art Unit	Examiner
1618	J. ROGERS

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal.

The review is requested for the reason(s) stated on the attached sheet(s).
Note: No more than five (5) pages may be provided.

I am the

☐ applicant/inventor.

☐ assignee of record of the entire interest.
See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed.
(Form PTO/SB/96)

☑ attorney or agent of record.
Registration number 39538.

☐ attorney or agent acting under 37 CFR 1.34.
Registration number if acting under 37 CFR 1.34 _____

James T. Eller, Jr.
Signature

James T. Eller, Jr.
Typed or printed name

703-205-8000
Telephone number

February 24, 2011
Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required.
Submit multiple forms if more than one signature is required, see below*.

☑ *Total of 3 forms are submitted.

This collection of information is required by 35 U.S.C. 132. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11, 1.14 and 41.6. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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Docket No.: 1599-0293PUS1
(Patent)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patent Application of:
Min-Hyo SEO et al.

Application No.:	10/554,637	Confirmation No.:	9196
Filed:	October 27, 2005	Art Unit:	1618
For:	BIODEGRADABLE BRANCHED POLYLACTIDE DERIVATIVES CAPABLE OF FORMING POLYMERIC MICELLES, AND THEIR PREPARATION METHOD AND USE	Examiner:	J. ROGERS

ARGUMENTS IN SUPPORT OF PRE-APPEAL BRIEF REVIEW

MS AF **February 24, 2011**
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

The Rejections

Claims 1, 3-4, 7-8 and 10-14 are rejected under 35 USC 103(a) as being unpatentable over Lee et al. (Journal of Polymer-Science, Part A: Polymer Chemistry, Vol. 39, 973-985, 2001) in view of Seo et al. (WO 03/033593). Claims 5 and 9 are rejected under 35 USC 103(a) as being unpatentable over Lee et al. in view of Seo et al. and in view of Sodergard (US 2004/0091573). These rejections are respectfully traversed.

Argument

The present invention relates to a micellar composition (and a method of preparing a branched polylactic acid derivative as distinguishable from a linear form) comprising a water-soluble branched polylactic acid derivative which can form stable micelles and increase the solubility of poorly water-soluble drugs by entrapping the drugs in micelles. The present

invention stabilizes micelles by increasing the molecular weight of the polymer which is used to form the micelles and accordingly lowering the critical micelle concentration (CMC). Thus, as shown in Table 1 on page 19 of the present application, the higher the polymeric molecular weight, the lower the CMC value, which means that a higher molecular weight can form stable micelles in an aqueous solution. If the CMC value is too high, more polymer is required to form micelles and then the micelles become unstable, which results in precipitation of poorly water-soluble drugs. If the molecular weight of a linear PLA salt increases, it becomes more difficult to dissolve in water. The present inventors have designed a multiarm polymer structure (branched structure) wherein the total molecular weight increases but that of each PLA arm does not, while the water solubility is maintained.

The present invention seeks to provide a stable micellar composition. In the Lee et al. reference, the degradation rate of COOH terminated polylactide is higher than those having other terminals, and among the COOH-terminated polylactides, 3- or 4-armed COOH-terminated PLA has a higher degradation rate than linear PLA (see the Abstract and Fig. 6). This is because the hydrolysis of the polymer backbone is accelerated by the presence of the terminal acid group (COOH), and accordingly 3- or 4-armed PLA, which has more acid groups, is degraded more rapidly (please see the right column, P982 of the Lee et al. reference).

However, the present invention relates to a micellar composition providing micelles with increased stability in order to entrap and maintain hydrophobic drugs therein. Furthermore, the terminal of the present polymer is in a salt form and not an acid form. The Lee et al. reference teaches away from the increased stability of the micelles in the present invention since the Lee et al. reference teaches that more accelerated degradation of the polymer can be achieved by more multi-arms of the polymer.

Lee discloses a molecular weight of 33,200 for its polymer (pages 978 and 983). Such a high molecular weight is far beyond the scope of the present polymer and is neither water soluble nor capable of forming micelles. Lee relates to a drug delivery for water-insoluble materials wherein the degradation rate, depending on terminal groups, is important. Lee does not pertain to the technical idea of forming stable micelles and entrapping poorly water-soluble drugs therein.

The Seo reference does not provide any teaching or suggestion as to whether the molecular weight of a linear PLA salt should increase, how to increase the molecular weight, and whether the water solubility would be maintained and micelles could be formed even if the molecular weight increases.

The Examiner also alleges that the micellar formation is obvious from the combination of the Lee et al. and Seo et al. references. However, the Seo et al. reference just mentions low-molecular weight and linear polymers. The Seo et al. reference fails to provide any expectation as to whether its polymer can maintain the water solubility when it becomes a multi-armed form with higher molecular weight. The Lee et al. reference discloses a water-insoluble and high molecular weight polymer having about 33,200 Daltons. Therefore, even if the prior art is combined, one skilled in the art could not have easily modified the molecular weight of the polymer to arrive at the present invention. Whether a polymer is soluble or insoluble in water should be regarded as an important factor of polymer properties. It is never a simple modification of numerical ranges or ratios. Thus, the compatibility of forming micelles in an aqueous solution within a specific molecular range defines an inventive contribution not recognized by either the Lee or Seo references.

The Sodergard reference relates to a chewing gum. In the Sodergard reference, biodegradable polymers are used as a gum base. That is, the technical field of the Soderguard reference is totally different from that of the present invention, i.e., drug delivery. In the Sodergard reference, it is not necessary for the polymer to entrap drugs therein at all. In addition, the polymer of the Sodergard reference is used for a gum base and thus should not be water soluble. One skilled in the art would never refer to the teachings of the Sodergard reference for developing a drug-delivery system.

The Examiner argues that the Sodergard reference was used as a secondary reference for its description on how to make PLA multiarm copolymers and not for its description of how to use such polymers (page 5 of the Office Action). However, the technical field of the Sodergard reference and the use of polymers prepared by the Sodergard referene are totally different from those of the present invention. Thus, the Sodergard reference would not be relevant for a skilled artisan to consider for developing a drug-delivery system. Furthermore, the Sodergard reference provides no teaching or suggestion concerning the use of polymers as drug delivery agents for

forming stable micelles. Thus, it is unlikely that the combination of the Sodergard polymer with the teachings of the Seo and Li references would be tried at all since the technical fields of the inventions are totally different. Furthermore, even if they were combined, such a combination provides no prediction, teaching, suggestion or motivation as to whether the molecular weight of the PLA salt should increase in order to increase micelle stability and whether the water solubility would be maintained and micelles could be formed even if the polymer is prepared in a multiarm form.

According to Experimental Example 1 of the present application, the branched polymer of the present invention can form micelles even when its molecular weight increases. Furthermore, according to Experimental Example 2 of the present invention, comparing PLA-COONa (1,140; 10% of drug) with 3-arm PLA-COONa (3,000; 10% of drug), the drug solubility increased from 20 to 27 mg/ml, which corresponds to a 35% increase in solubility. Such a remarkable effect of the present invention (i.e., increasing drug solubility as well as micelle stability) would not be expected from any of the Seo, Lee or Sodergard references.

Accordingly, in view of the above remarks, reconsideration of the rejections and allowance of all of the claims of the present application are respectfully requested.

Dated: February 24, 2011

Respectfully submitted,

By _____

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